The National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria, 1996-1999: surveillance for action

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The National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria was initiated in 1996 as a collaboration between the National Center for Infectious Diseases at the Centers for Disease Control (CDC), United States Food and Drug Administration Center for Veterinary Medicine (FDA-CVM), the Agricultural Research Service, Food Safety and Inspection Service, and the Animal Plant Health Inspection Service of the United States Department of Agriculture (USDA).[1,2] Bacterial isolates from humans are currently provided by 17 state and local public health laboratories. The purpose of NARMS is to prospectively monitor antimicrobial resistance in isolates of selected enteric bacteria collected from humans, animals, and animal products. The goals of NARMS are to provide descriptive data on the extent and temporal trends of antimicrobial resistance in enteric organisms from the human and animal populations; provide timely information to veterinarians and physicians; prolong the life span of approved drugs by promoting the prudent use of antimicrobial agents; identify areas for more detailed investigation; and guide research on antimicrobial resistance. This paper addresses NARMS surveillance conducted at CDC from 1996 through 1999.

Materials and Methods

The total population in 17 NARMS sites (California, Connecticut, Colorado, Florida, Georgia, Kansas, Massachusetts, Maryland, Minnesota, New Jersey, New York, Oregon, Tennessee, Washington, West Virginia, Los Angeles County, and New York City) in 1998 was 103 million people, or 38% of the United States population. Since 1996, NARMS has conducted surveillance for antimicrobial resistance among isolates of nontyphoidal *Salmonella*. In 1997, surveillance was expanded to include human isolates of *Campylobacter*.

Clinical laboratories isolate *Salmonella* or *Campylobacter* from patient specimens. *Salmonella* are isolated from blood, feces, urine, or other specimens; *Campylobacter* isolates are obtained from fecal specimens only. Most clinical laboratories in participating sites submit almost all *Salmonella*, but few submit *Campylobacter* isolates to state or local public health laboratories. Serotyping of *Salmonella* isolates is done at the submitting state public health laboratory. Participating state and local public health laboratories submit every 10th nontyphoidal *Salmonella* isolate and one *Campylobacter* isolate per week to CDC for susceptibility testing.

At CDC, isolates are tested for susceptibility using minimum inhibitory concentrations (MIC). *Salmonella* isolates are tested with a semi-automated system' for susceptibility to 17 antimicrobial agents. Campy lobacter isolates are tested using the E-test system[b] for susceptibility to 8 antimicrobial agents. Data are analyzed by a SAS system.[c]

Results

From 1996 through 1999, 5,592 NARMS *Salmonella* isolates were serotyped and tested for susceptibility. In 1999, the most frequently isolated serotypes included 5

Typhimurium (24%) and *S. enteritidis* (18%). Other common serotypes included S Newport (6.5%), *S Heidelberg* (6%), *S. Montevideo* (3.5%), *S Muenchen* (3.4%), and *S Javiana* (2.8%). Other serotypes accounted for 36% of isolates and included 120 other serotypes. Antimicrobial resistance is more common in some serotypes than others. In 1999, all 5 Hadar isolates and 51% of *S Typhimurium* isolates were resistant to > 1 agent, whereas only 2.4% of *S Javiana* isolates were resistant to > 1 agent. In 1999, 26% of *Salmonella* isolates were resistant to > 1 antimicrobial agent. Although most *Salmonella* isolates remain susceptible to the 17 antimicrobial agents tested, several concerning trends in antimicrobial resistance among *Salmonella* are evident. These include multi-drug resistance, highly resistant isolates, and the emergence of resistance to ceftriaxone and fluoro-quinolones, which are antimicrobial agents commonly used to treat people with *Salmonella* infections.

Increasing multiresistance is most evident within certain serotypes, particularly *S Typhimurium*. In 1999, 28% of *S Typhimurium* isolates were resistant to ampicillin, chloramphenicol, streptomcyin, sul-famethoxazole, and tetracycline (R-type ACSSuT), the characteristic pattern of Definitive Phage Type 104, Some *S Typhimurium* R-type ACSSuT isolates were also additionally resistant to kanamycin (11.8%), cephalothin (8.8%), amoxicillin/clavulanic acid (6.9%), trimethoprim-sulfamethoxazole (6.9%), ceftio-fur (2.9%), and ceftriaxone (1%). Another penta-resis-tant pattern is prevalent among *S Typhimurium* isolates; resistance is to ampicillin, kanamycin, streptomycin, sulfamethoxazole, and tetracycline (R-type AKSSuT). The percentage of *S Typhimurium* isolates with this pattern increased from 4.5% in 1996 to 11% in 1999, making it the second most common multi-drug resistant pattern.

From 1996 through 1999, 59 (1.1%) of 5592 *Salmonella* isolates were highly resistant, that is, resistant to > 8 of 17 antimicrobial agents. Among highly resistant *Salmonella*, 42% were *S Typhimurium* and 39% were S Newport. Other serotypes included S Berta, S Stanley, and S Paratyphi-A. The most resistant isolate in the NARMS collection was an S Typhiumurium variant Copenhagen isolate; it was susceptible only to apramycin, amikacin, and ciprofloxacin.

Since 1996, 22 *Salmonella* isolates were identified with resistance to ceftriaxone, an extended-spectrum cephalosporin. Most of these isolates were *S Typhimurium*. The percentage of *Salmonella* isolates with decreased susceptibility to ciprofloxacin (MIC >. 0.25µg/ml) has increased since 1996. The percentage of isolates with decreased susceptibility to ciprofloxacin was 0.4% in 1996, 0.6% in 1997, 0.7% in 1998, and 1.0% in 1999. These data included two ciprofloxacin-resistant isolates from 1998 to 1999.

From 1997 through 1999, 881 *Campylobacter* isolates were tested; 60% of *Campylobacter* isolates were resistant to > 1 agent; 25% were resistant to > 2 agents. Of concern, the percent of *Campylobacter* isolates resistant to ciprofloxacin increased from 13% in 1997 to 18% in 1999.

Discussion

Since 1996, NARMS has accumulated information on antimicrobial resistance among *Salmonella* and *Campylobacter* isolates collected from humans. Among *Salmonella* isolates, several multi-drug resistant strains are prevalent, particularly *S Typhimurium* R-type ACSSuT and AKSSuT. There is also emergence of resistance to

antimicrobial agents that are commonly used to treat people with *Salmonella* infections (ceftriaxone and ciprofloxacin).

Increasing resistance to ciprofloxacin is also evident among *Campylobacter* isolates.

The public health utility of NARMS data is wide-ranging; the data have supported field investigations of outbreaks of illness marked by a pathogen that displayed an unusual antimicrobial resistance pattern, provided data for a risk assessment of the human health impact of fluoroquinolone use in poultry, stimulated research in molecular characteristics of resistance emergence and transfer, improved knowledge of risk factors associated with the development of an antimicrobial-resistant infection, and triggered broader research projects of prudent antimicrobial use in animals and the role of the environment in the emergence and spread of antimicrobial resistance.

For example, the FDA recently proposed to withdraw approval of the use of fluoroquinolones in poultry based on their risk assessment.[3] The risk assessment concluded that the use of fluoroquinolones in poultry causes the development of fluoroquinolone-resistant Campyiobacter in poultry, which is transferred to humans, compromising the use of fluoroquinolones for the treatment of human Campvlobacter infections. The FDAs action is based on data from NARMS and other sources. This example, and others, demonstrate that the NARMS multi-agency collaboration has brought the problem of antimicrobial resistance to the forefront; it is indeed "surveillance for action."

[a]Sensititre, Trek Diagnostics, Westlake, Ohio.
[b]E-test system, AB Biodisk, Solna, Sweden.
[c]SAS, version 6.12, SAS Institute, Cary, NC.

References

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